

AFICAMTEN AND MAVACAMTEN: WHEN SIDE EFFECTS AFFECT EFFICACY

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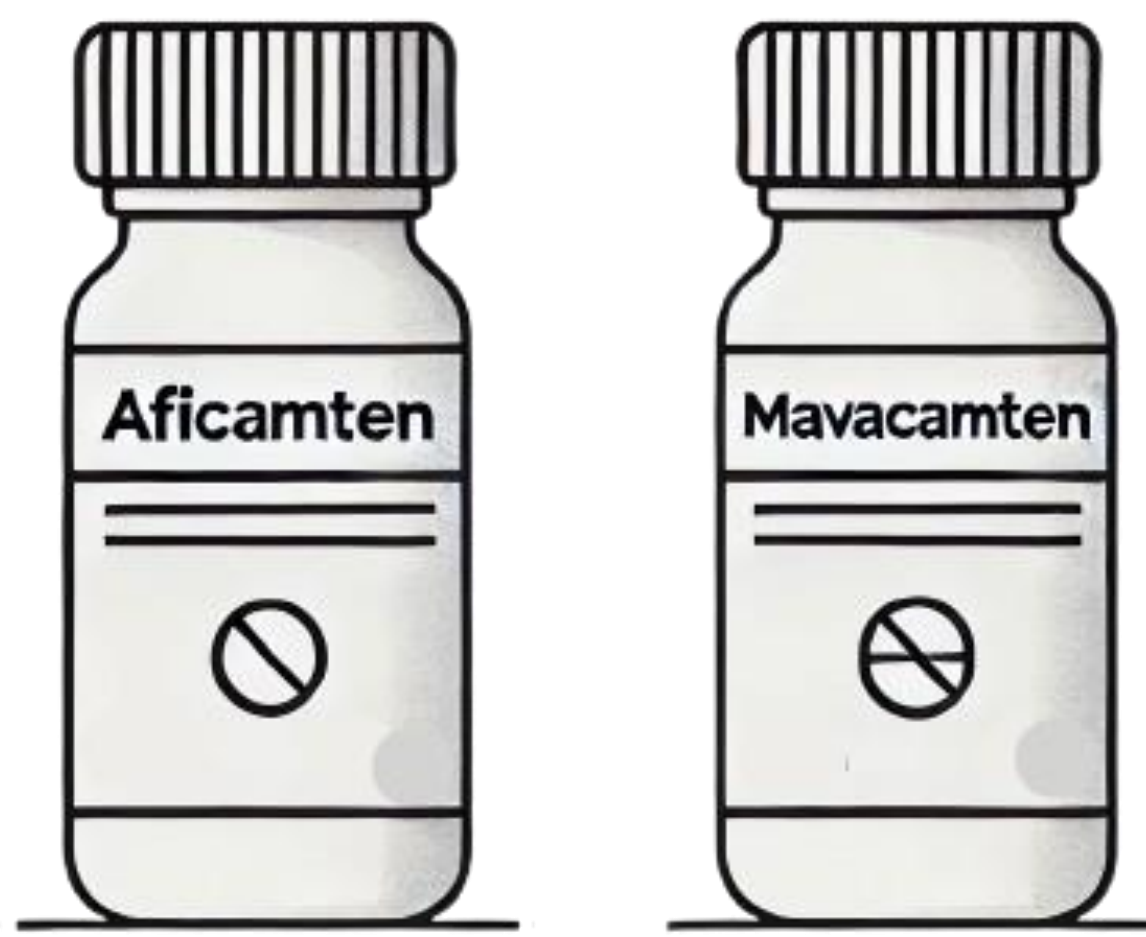
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BACKGROUND

Adjusted **Hazard Ratios** for Peak VO₂ and Ejection Fraction (LVEF) in **Coats' Regression for Death and Transplant**

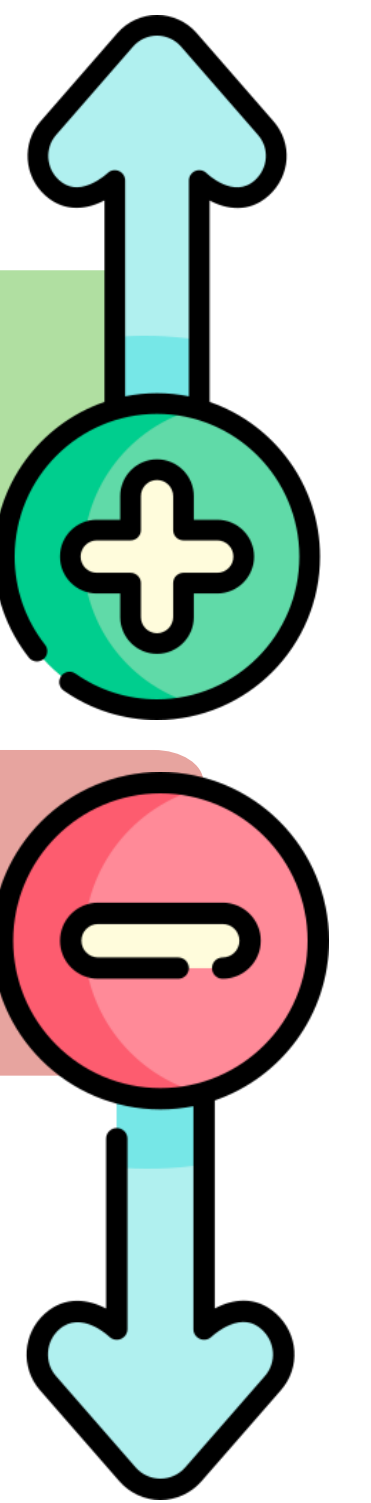
Exercise Variables	Death or Transplant (n=178)	Death (n=156)	Transplant (n=22)
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Peak VO ₂	0.82 (0.77, 0.88)	0.82(0.77, 0.88)	0.87 (0.79, 0.96)
Ejection Fraction	0.00003 (1.67e ⁻⁸ , 0.081)	0.005 (3.46e ⁻⁷ , 62.06)	7.59e ⁻¹¹ (1.33e ⁻¹⁷ , 0.0004)

(Coats et al., 2015)



INCREASE pkVO₂

DECREASE LVEF



AIM AND OBJECTIVES

To evaluate, using the centered prognostic index (CPI) from Coats et al.'s equation, the impact of pkVO₂ increase from mavacamten and aficamten, first without considering the variation in LVEF, and then taking this variation into account.

MATERIALS AND METHODS

Clinical Trial > N Engl J Med. 2024 May 30;390(20):1849-1861. doi: 10.1056/NEJMoa2401424.

Epub 2024 May 13.

Aficamten for Symptomatic Obstructive Hypertrophic Cardiomyopathy

Clinical Trial > Lancet. 2020 Sep 12;396(10253):759-769. doi: 10.1016/S0140-6736(20)31111-1.

Epub 2020 Aug 29.

Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial

- Increase in PKVO₂
- Mean change in LVEF
- Hazard Ratios from Coats et al.'s equation → Coefficients

CPI was first calculated based on the pkVO₂ and then incorporating LVEF

$$CPI = b_1(x_1 - \bar{x}_1) + \dots + b_p(x_p - \bar{x}_p) = \sum b_i x_i - \sum b_i \bar{x}_i$$

RESULTS

pkVO₂ increase:

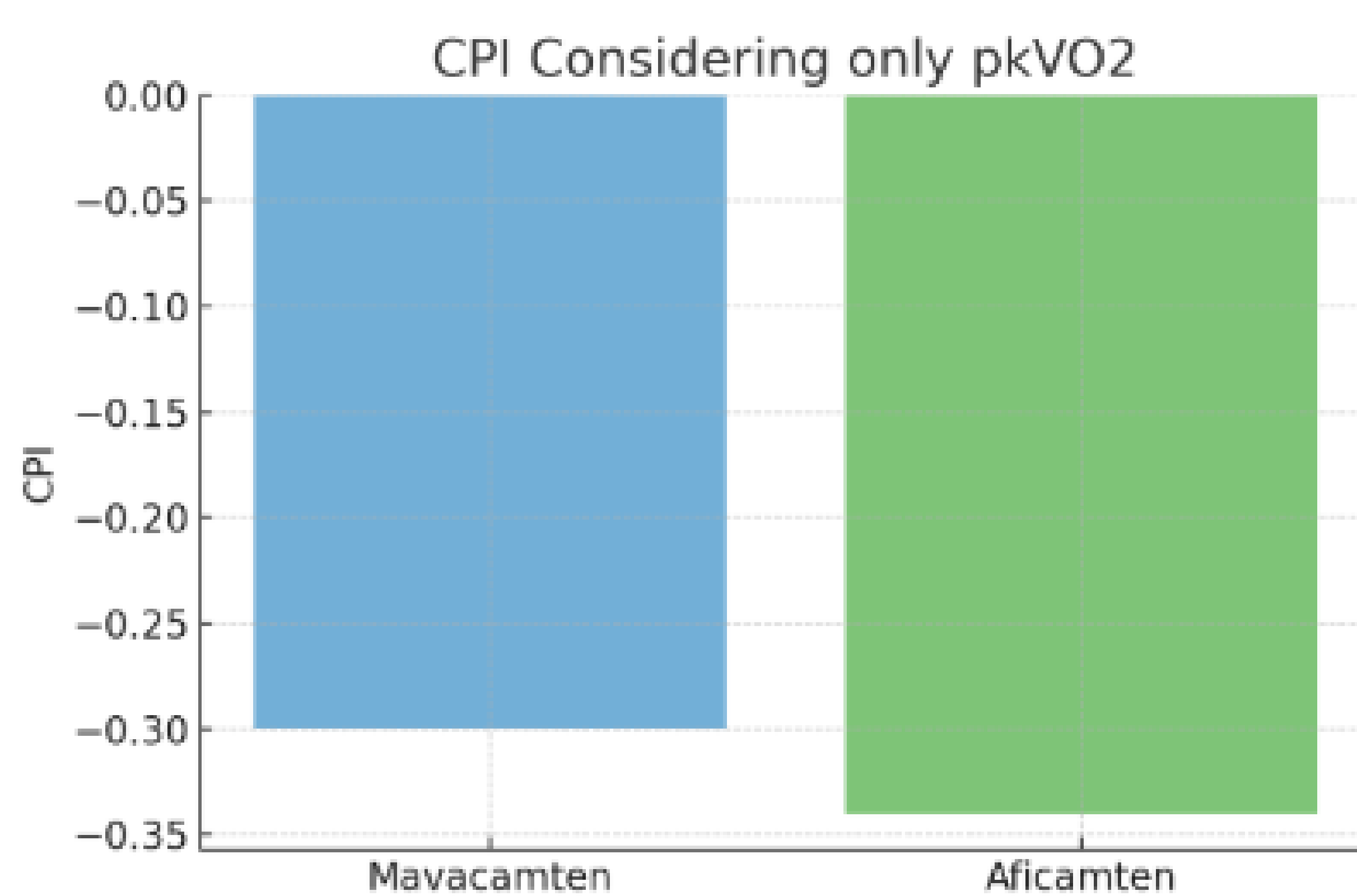
- 1.5 ml/kg/min mavacamten
- 1.7 ml/kg/min aficamten

Reductions in LVEF:

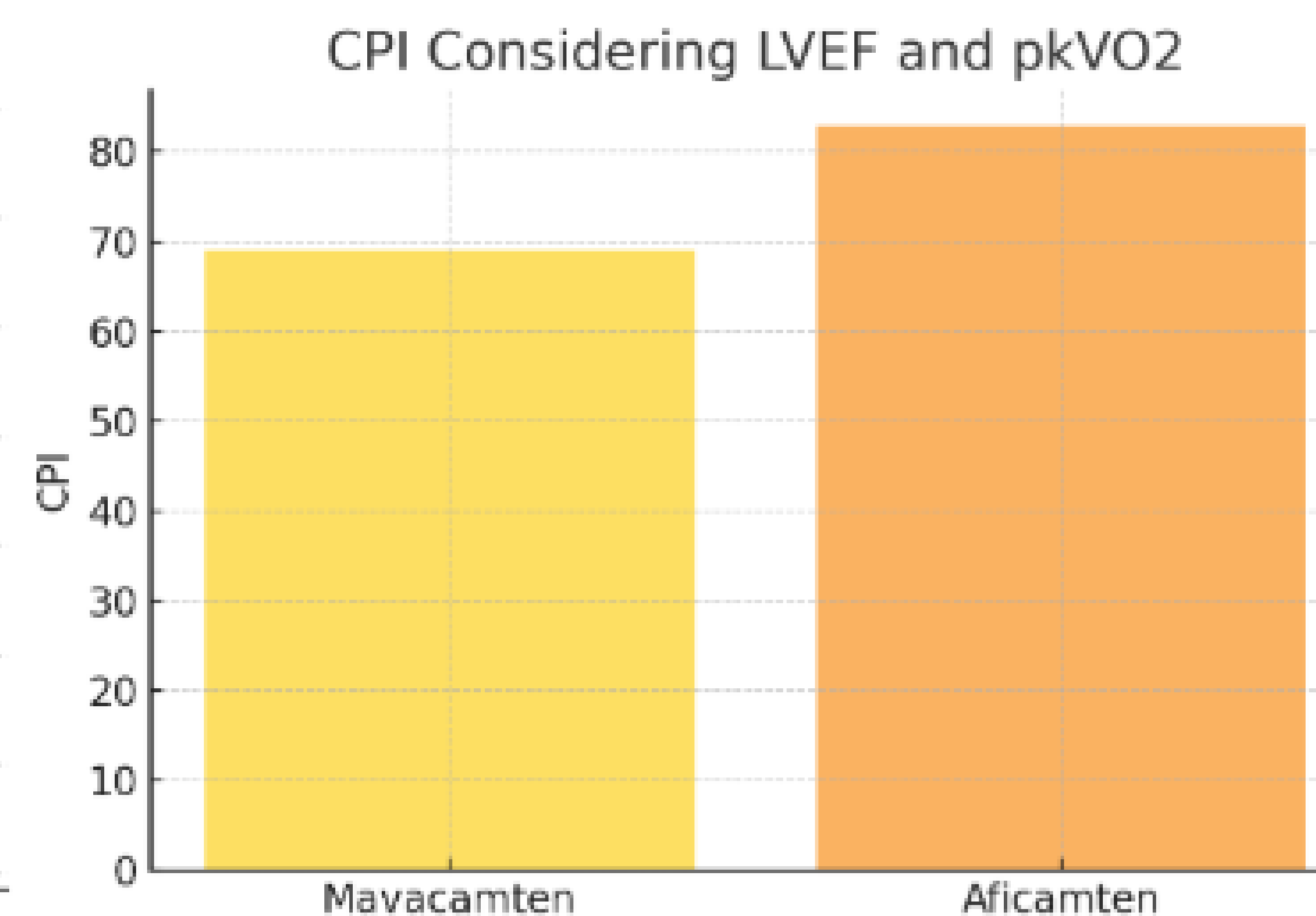
- 4.0 percentage points mavacamten
- 4.8 percentage points aficamten

Coefficients:

- -0.198 for pkVO₂
- -17.32 for LVEF



favorable prognosis



worse prognosis

CONCLUSIONS

According to Coats et al.'s equation, the pkVO₂ increase is initially associated with a better prognosis when other variables are held constant. However, **when the reduction in LVEF is also taken into account, the prognosis worsens. It cannot be concluded from this data that the use of these drugs reduces death or transplantation risk.**

6ER-008
ATC: C01



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